Future Plans

Product Management in Proteomics and Developing New Global Protein Purification Products (Promega)

Executive Coach and Keynote Speaker for Professional and Career Development for Graduate Students/PhDs/Postdocs

Scientific Recruitment Consultant

Entrepreneur

WISCONSIN
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Cellular and Molecular Pathology

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Cellular and Molecular Pathology

Ryan Raver

Program of the Thesis Defense Seminar for the
Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

"The Role of the B-cell Specific Transcription Factor, Pax5, in EBV Latency and Lytic Reactivation"

Tuesday, July 30, 2013, 1 pm
11th Floor, Temin Room,
McArdle Cancer Research Center

Research conducted in the lab of
Shannon Kenney, MD
Department of Oncology

Ryan Raver's Thesis Abstract

The Role of the B-cell Specific Transcription Factor, Pax5, in EBV Latency and Lytic Reactivation

Ryan Raver
Under the supervision of
Professor Shannon Kenney, MD
at the University of Wisconsin-Madison

EBV is associated with several B-cell and epithelial cell cancers, including Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma (NPC), and gastric carcinoma. However, to be transmitted from host to host, and from cell to cell, the virus periodically reactivates from latency and converts to the lytic form of replication. The latent-to-lytic switch of EBV in host cells is controlled at the level of the BZLF1 and BRLF1 viral immediate-early promoters and their associated gene products, Z and R, which are transcription factors. However, cellular factors which regulate the latent-to-lytic switch remain incompletely characterized. Here I investigate the role of the B-cell specific transcription factor and master regulator, Pax5, in promoting EBV latency. Pax5 is known to play an essential role in allowing EBV to establish long-term latent infection in B cells, since it binds to and activates an essential EBV latency promoter, Wp, that drives expression of the viral EBNA2 and EBNA-LP proteins during primary B-cell infection. I demonstrate that Pax5 attenuates the function of the major lytic switch protein, Z, by inhibiting Z transcriptional function and DNA binding activity, and thereby prevents lytic reactivation. Thus, I have uncovered a new mechanism by which Pax5 helps to promote EBV latency in B cells, by blocking Z function. In addition, I demonstrate that Pax5 binds directly to the terminal repeat region of the EBV genome and may positively regulate expression of the major EBV oncogene, LMP1. In conclusion, these results reveal novel mechanisms by which the Pax5 cellular transcription factor promotes B-cell specific viral latency.

Publications

Raver, R.M., A.R. Panfil, S.R. Hagemeier, and S.C. Kenney. 2013. The B-cell Specific Transcription Factor and Master Regulator, Pax5, Promotes EBV Latency by Negatively Regulating the Viral Immediate Early Protein, BZLF1. J Virol.

Raver, R.M., C.K.Wille, E.A. Barlow, E.C. Johannsen, and S.C. Kenney. The B-cell Specific Transcription Factor, Pax5, Regulates LMP1 Expression, via Binding to the Epstein-Barr Virus Terminal Repeats. Manuscript In Progress.

Honor & Awards

CMP T32 NIH Training Grant/Fellowship

Wisconsin Entrepreneurial Bootcamp (WEB) Alumni (2012)

Featured Speaker for "Effective Networking - Building a Power Network" at the UW-Madison Post-Doctoral Conference on Professional Development (2013).